REMARKS

Claim 1 has been amended. Claims 20-22 have been added. Thus, claims 1-3 and 8-22 are pending in this application. No new matter has been added by way of these amendments because each amendment is supported by the present specification. For example, the amendment to claim 1 has support in the specification at page 2. New claims 20-22 are supported by original claims 1-3. Thus, no new matter has been added.

Applicants respectfully submit that the present specification has been checked for errors, and believe that no amendments are necessary. With regard to the term "etc." in the specification, one skilled in the art would understand this term and the written description without the aid of any outside source.

Based upon the above considerations, entry of the present amendment is respectfully requested.

In view of the following remarks, Applicants respectfully request that the Examiner withdraw all rejections and allow the currently pending claims.

Issues under 35 U.S.C. §§ 101 and 112, First Paragraph

Claims 1-3 stand rejected under 35 U.S.C. § 101 because the claimed invention is asserted to not have patentable utility. Also, claims 1-3 stand rejected under 35 U.S.C. § 112, first

paragraph, because the specification is asserted to not enable for diseases other than arteriosclerosis. Applicants respectfully traverse.

With regard to utility of the present invention, the Office Action states that no evidence of prevention has been provided (at page 5 of the Office Action). However, Applicants respectfully submit that the present specification demonstrates a patentable utility for the present invention.

Figure 1 depicts the experimental results when using the present invention in treating and preventing diseases. The 2,5,7,8-tetramethyl-2-(β-carboxyethyl)-6-hydroxychromane ("α-CEHC") and 2,7,8-trimethyl-2-(β-carboxyethyl)-6-hydroxychromane ("γ-CEHC") compounds clearly block attack by the oxidation starter, V-70 (described in the paragraph bridging pages 6-7 of the specification), to LDL during a lag-time (as shown in Figure 1).

The prolonged lag-times achieved by the present invention demonstrate the anti-oxidative effects of the claimed α-CEHC and γ-CEHC compounds on LDL. As explained in the paragraph bridging pages 7-8, the control group had a lag-time of 88.1 ± 29.4 minutes, versus 190.8 ± 65.1 minutes for α-CEHC and 263.1 ± 114.8 for γ-CEHC. Thus, both α-CEHC and γ-CEHC treat heart disease and arterial sclerosis by blocking or inhibiting the progress of this disease and condition due to the inhibition of oxidized LDL.

Further, because of the block in initiation of arteriosclerosis that is triggered by oxidized LDL, both of the α-CEHC and γ-CEHC compounds prevent the onset of arteriosclerosis. Therefore, α-CEHC and γ-CEHC are effective in preventing and treating heart disease and arterial sclerosis.

Thus, the present invention has a patentable utility, whereby the present specification fully describes such utility. Applicants respectfully request withdrawal of the rejection under § 101.

With regard to the issue of enablement, Applicants respectfully submit that claim 3 and claim 22 are directed to the disease of arteriosclerosis. Thus, Applicants respectfully request that the Examiner declare that the present specification (Office Action refers to page 3, line 1) enables the scope of at least claims 3 and 22.

With respect to the other presently pending claims, one skilled in the art could readily make and use the present invention without undue experimentation. The Examiner refers Applicants to page 3, line 1 of the present specification to show that the specification discloses arteriosclerosis.

However, Applicants respectfully submit that other diseases are disclosed (*i.e.*, heart disease at page 9, line 3).

Further, Applicants note that the initial burden of establishing a *prima facie* basis to deny patentability to a claimed

invention on any ground is always upon the examiner." *Ex parte* Parks, 30 USPQ2d 1234, 1236 (citing In *re Oetiker*, 24 USPQ2d 1443 (Fed. Cir. 1992)). Here, the Examiner has not established a *prima facie* case of nonenablement because the Examiner has not provided "acceptable evidence of nonenablement". *See Utter v. Hiraga*, 6 USPQ2d 1709, 1714 (Fed. Cir. 1988) (That some experimentation is necessary does not preclude enablement, however, unless the amount of experimentation is unduly extensive); *In re Wright*, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). For the present application, one having ordinary skill in the art could make or use the present invention based on the present written description and coupled with information known in the art without undue experimentation.

For example, one skilled in the art would read all of the present specification, including the experimental data in the specification (*i.e.*, Figure 1 and the paragraph bridging pages 7-8 explaining the significance of the lag-times of the control group, α-CEHC and γ-CEHC), and understand what is being claimed. Given this information, one having ordinary skill in the art could make or use the present invention based on the present written description and coupled with information known in the art without undue experimentation. The Examiner has not presented any acceptable evidence or reasoning that would counter or be inconsistent with the present specification. Without acceptable

evidence or reasoning, the Examiner must take the present disclosure as complying with 35 U.S.C. § 112, first paragraph.

Thus, the Examiner has not met the initial burden of establishing a reasonable basis to question the enablement. Therefore, Applicants respectfully request the Examiner to withdraw this rejection.

Applicants further submit that a proper analysis for enablement (or lack thereof) would require a weighing of the various *Wands* factors. 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). With a proper weighing of the *Wands* factors, any question of enablement for the full scope of a claim is determined from the perspective of one having ordinary skill in the art.

However, *In re Wands* has not even been cited in the Office Action, nor is there any proof that there is a lack of enablement present for the instantly pending claims. Also, because one skilled in the art would understand the significance of the lag-times for α-CEHC and γ-CEHC, that person skilled in the art would know how to make and use the present invention with regard to other diseases or conditions (*i.e.*, by blocking or inhibiting the progress of this disease and condition due to the inhibition of oxidized LDL). No evidence has been provided to counter this scientific evidence.

Thus, Applicants respectfully submit that the present specification fully enables one skilled in the art to make and use the present invention. Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw this rejection.

Issues under 35 U.S.C. § 112, Second Paragraph

Claims 1-3 stand rejected under 35 U.S.C. § 112, second paragraph, due to reasons of indefiniteness. Applicants respectfully traverse.

The Office Action states that the claim language of "preventing" is vague and subjective. However, Applicants respectfully note that the proper perspective for determining the scope of the presently pending claims is one having ordinary skill in the pertinent art. Here, prevention of a disease or condition means preventing the onset of that disease or condition, and one skilled in the art would understand this. Applicants also refer the Examiner to their previous comments with regard to preventing a disease or condition and disclosure in the specification (under "Issues under 35 U.S.C. §§ 101 and 112, first paragraph").

With regard to "at least one" present in claim 1, Applicants respectfully refer the Examiner to the amended claim whereby this claim language is no longer present. In claim 1, a Markush group is properly recited.

Thus, based on the above remarks, Applicants respectfully request the Examiner to reconsider and withdraw this rejection.

A full and complete response has been made to all issues as cited in the Office Action. Thus, Applicants respectfully request that the Examiner pass the application to issue.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Eugene T. Perez (Reg. No. 48,501) at the telephone number of the undersigned below.

Attached hereto is a marked-up version of the changes made to the application by this Amendment.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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JWB/ETP:bmp
0425-0854P

Attachment: Version with Markings to Show Changes Made

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE ABSTRACT OF THE DISCLOSURE:

The Abstract of the Disclosure has been amended as follows:

The present invention provides a method of preventing or treating a disease caused by oxidation [in vivo] *in vivo* by administering a pharmacologically effective amount of at least one compound selected from the group consisting of: [¶]

[(1)2,5,7.8-tetramethyl-2-(β-carboxyethyl)-6-hydroxychromane;] (1) 2,5,7,8-tetramethyl-2-(β-carboxyethyl)-6-hydroxychromane; and [¶]

[(2) 2,7.8-trimethyl-2-(β-carboxyethyl)-6-hydroxychromane.] (2) 2,7,8-trimethyl-2-(β-carboxyethyl)-6-hydroxychromane. [¶]

Further, it provides use of a compound selected from the group consisting of (3) α-tocopherol, (4) α-tocotrienol, (5) γ-tocopherol and (6) γ-tocotrienol for generation *in vivo* of any of the above compounds (1) and (2) to treat a disease caused by oxidated low density lipoprotein (LDL).

[As the above-mentioned disease, arteriosclerosis is particularly preferred.]

IN THE CLAIMS:

The claims have been amended as follows:

Claim 1. (Twice Amended) A method of [preventing or] treating a disease caused by oxidation in vivo, said method comprising a step of administering a pharmacologically effective amount of [at least one] a compound selected from the group consisting of:

(1) 2,5,7,8-tetramethyl-2-(β-carboxyethyl)-6-hydroxychromane, a pharmacologically acceptable salt thereof, or a pharmacologically acceptable hydrate thereof; and

(2) 2,7,8-trimethyl-2-(β-carboxyethyl)-6-hydroxychromane, a pharmacologically acceptable salt thereof, or a pharmacologically acceptable hydrate thereof.

Claims 20-22 have been added.

ABSTRACT OF THE DISCLOSUSRE

The present invention provides a method of preventing or treating a disease caused by oxidation *in vivo* by administering a pharmacologically effective amount of at least one compound selected from the group consisting of: (1) 2,5,7,8-tetramethyl-2-(β-carboxyethyl)-6-hydroxychromane; and (2) 2,7,8-trimethyl-2-(β-carboxyethyl)-6-hydroxychromane. Further, it provides use of a compound selected from the group consisting of (3) α-tocopherol, (4) α-tocotrienol, (5) γ-tocopherol and (6) γ-tocotrienol for generation *in vivo* of any of the above compounds (1) and (2) to treat a disease caused by oxidated low density lipoprotein (LDL).